Professor Baker received his undergraduate degree from Harvard University in 1984. He obtained his doctorate in 1989 from the University of California, Berkeley, in the laboratory of Randy Schekman, where he worked predominantly on protein transport and trafficking in yeast. He spent three years as a post-doctoral fellow in the Department of Biochemistry and Biophysics, UCSF, in the laboratory of David Agard, where he developed a keen understanding of the computational basis of structure determination by crystallographic methods and began to develop his own computational approaches to structural analysis and prediction. In 1993 Dr. Baker joined the faculty of the Department of Biochemistry at the University of Washington, Seattle, thereby returning to his home turf. At the University of Washington, Professor Baker's group developed the Rosetta algorithm for ab initio protein structure prediction, which has been extended to a distributed computing project called Rosetta@Home.

Rather than attempting a physical model for local sequence-structure relationships, the Rosetta approach uses the database of known three-dimensional protein structures to provide sample structures of short sequence segments that correspond to sequences in the unknown structure. The distribution of local structures adopted by the database segments is taken as an approximation to the distribution of structures sampled by the unknown structures and energy calculations are then used to determine the non-local interactions that lead to a minimum energy configuration. This can then be used as a starting point for further refinements. The Rosetta project aims to produce structural models for protein complexes as well as individual polypeptide chains. The Baker group participates regularly and has had outstanding success in the biennial CASP (Critical Assessment of techniques for protein Structure Prediction) competition using ab initio methods. The Baker group is also active in the field of protein design and provided the first example of a designed protein, known as Top7, with an entirely novel fold.

Although now known best for their computational work, the Baker group has always maintained an active experimental component, which has provided essential input for the database of their prediction and design algorithms.

Professor Baker has been a Howard Hughes Medical Institute Assistant Investigator since 2000. Among many recognitions, he has received the Irving Sigal Young Investigator Award from the Protein Society, the Overton Award from the International Society of Computational Biology, and the AAAS Newcomb Cleveland Prize. Professor Baker is also a recipient of the Feynman Prize from the Foresight Institute and was elected a member of the National Academy of Sciences in 2006.